Refine Search

Search Results -

Terms	Documents
L3 and L6	0

Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L11

Refine Search | Recall Text | Clear | Interrupt

Search History

DATE: Tuesday, April 17, 2007 **Purge Queries** Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ			
L11	L3 and L6	0	L11
L10	L3 and L2	16	L10
L9	L3 and L7	0	L9
L8	UL48 adj mutation	0	L8
L7	Vmw65 adj mutation	14	L7
L6	VP16 adj mutation	2	L6
L5	L3 and substitute	3	L5
L4	L3 and "non-HSV VP16"	0	L4
L3	L2 and VP16	16	L3
L2	L1 and "herpes simplex virus"	117	L2
L1	435/91.4.ICLS.	437	L1

END OF SEARCH HISTORY

WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Tuesday, April 17, 2007

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L14	L13 and VP16	13
☐	L13	L12 and L2	99
☐	L12	435/320.1.ICLS.	32647
☐	L11	L3 and L6	0
☐	L10	L3 and L2	16
☐	L9	L3 and L7	0
☐	L8	UL48 adj mutation	0
☐	L7	Vmw65 adj mutation	14
☐	L6	VP16 adj mutation	2
☐	L5	L3 and substitute	3
☐	L4	L3 and "non-HSV VP16"	0
☐	L3	L2 and VP16	16
☐	L2	L1 and "herpes simplex virus"	117
☐	L1	435/91.4.ICLS.	437

END OF SEARCH HISTORY

Connecting via Winsock to STN

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 4	DEC 18	CA/CAplus patent kind codes updated
NEWS 5	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 6	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 7	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 8	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 9	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 10	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 11	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 12	JAN 22	CA/CAplus updated with revised CAS roles
NEWS 13	JAN 22	CA/CAplus enhanced with patent applications from India
NEWS 14	JAN 29	PHAR reloaded with new search and display fields
NEWS 15	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS 16	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS 17	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS 18	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS 19	FEB 26	MEDLINE reloaded with enhancements
NEWS 20	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS 21	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS 22	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS 23	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS 24	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS 25	MAR 16	CASREACT coverage extended
NEWS 26	MAR 20	MARPAT now updated daily
NEWS 27	MAR 22	LWPI reloaded
NEWS 28	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS 29	MAR 30	INPADOCDB will replace INPADOC on STN
NEWS 30	APR 02	JICST-EPLUS removed from database clusters and STN

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

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FILE 'HOME' ENTERED AT 13:37:12 ON 17 APR 2007

=> caplus
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> STN biosis
AT LEAST TWO FILES ARE NEEDED FOR STNINDEX
SESSION CONTINUES IN THE PREVIOUS FILE ENVIRONMENT
To see a list of files and clusters that may be used in the INDEX command, enter HELP FILE NAMES or HELP CLUSTER NAMES at an arrow prompt. Only the learning files and NBSFLUIDS may not be used in STNINDEX.

=> caplus
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> HSV
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> Caplus
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> biosis
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:n

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.63	0.63

FILE 'CAPLUS' ENTERED AT 13:38:44 ON 17 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 17 Apr 2007 VOL 146 ISS 17
FILE LAST UPDATED: 15 Apr 2007 (20070415/ED)


```
=> (herps simplex virus)
             8 HERPS
             1 HERPSES
             9 HERPS
                 (HERPS OR HERPSES)
         26139 SIMPLEX
            99 SIMPLEXES
         26198 SIMPLEX
                 (SIMPLEX OR SIMPLEXES)
        359555 VIRUS
         76044 VIRUSES
        373007 VIRUS
                 (VIRUS OR VIRUSES)
L1           4 (HERPS SIMPLEX VIRUS)
                 (HERPS(W)SIMPLEX(W)VIRUS)

=> HSV
         12287 HSV
            56 HSVS
L2       12290 HSV
                 (HSV OR HSVS)

=> VP16 (1) deletion
          2244 VP16
         93456 DELETION
         28231 DELETIONS
        107069 DELETION
                 (DELETION OR DELETIONS)
L3         147 VP16 (L) DELETION

=> Vmw65 (1) deletion
           349 VMW65
         93456 DELETION
         28231 DELETIONS
        107069 DELETION
                 (DELETION OR DELETIONS)
L4          18 VMW65 (L) DELETION

=> VP16 (1) mutation
          2244 VP16
        253006 MUTATION
        165855 MUTATIONS
        315656 MUTATION
```

```
                (MUTATION OR MUTATIONS)
L5          226 VP16 (L) MUTATION

=> Vmw65 (l) mutation
            349 VMW65
         253006 MUTATION
         165855 MUTATIONS
         315656 MUTATION
                (MUTATION OR MUTATIONS)
L6           28 VMW65 (L) MUTATION

=> L2 and L3
L7           28 L2 AND L3

=> L2 and L5
L8           46 L2 AND L5

=> L2 and L4
L9            9 L2 AND L4

=> L2 and L6
L10          19 L2 AND L6

=> substitut4
L11     5563028 4

=> L11 and L7
L12           9 L11 AND L7

=> L11 and L8
L13          11 L11 AND L8

=> L11 and L10
L14           5 L11 AND L10

=> L11 and L7
L15           9 L11 AND L7

=> D L14 IBIB ABS 1-5

L14  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2001:472957  CAPLUS
DOCUMENT NUMBER:          135:56907
TITLE:                    Replication incompetent herpes viruses for use in gene
                          therapy of peripheral nervous system disorders
INVENTOR(S):              Coffin, Robert Stuart
PATENT ASSIGNEE(S):       Biovex Ltd., UK
SOURCE:                   PCT Int. Appl., 36 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     --------------       ----   --------    -------------------     --------
     WO 2001046450         A1    20010628    WO 2000-GB4983          20001222
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
```

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2395578	A1	20010628	CA 2000-2395578		20001222
EP 1246930	A1	20021009	EP 2000-985689		20001222
EP 1246930	B1	20051109			

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2003518081	T	20030603	JP 2001-546946		20001222
AT 309384	T	20051115	AT 2000-985689		20001222
AU 783691	B2	20051124	AU 2001-22088		20001222
US 2003040500	A1	20030227	US 2002-168801		20020911
PRIORITY APPLN. INFO.:			GB 1999-30419	A	19991222
			WO 2000-GB4983	W	20001222

AB The invention relates to replication incompetent herpes simplex viruses (HSV) capable of efficiently transferring genes to multiple sites within the nervous system for use in gene therapy. Highly disabled HSV vectors which cannot replicate in any cell other then those used to prepare vector stocks (i.e. essential genes have been inactivated in the vector which are complemented in the producer cell line) can give highly efficient gene delivery to the peripheral nervous system following direct injection into peripheral nerve. A replication incompetent HSV comprises: (a) a mutation which prevents or reduces the expression of at least two immediate early genes; and (b) a heterologous gene, which encodes a therapeutic protein, operably linked to a promoter active during herpes virus latency. The invention provides use of a replication incompetent HSV in the manufacture of a medicament for use in treating or preventing a peripheral nervous system disorder by administering said medicament to a peripheral nerve, in a method of determining whether a transgene has an effect on a phenotype associated with a peripheral nervous system disorder and in a method of treatment of a disorder of the peripheral nervous system.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:106039 CAPLUS

DOCUMENT NUMBER: 128:163659

TITLE: Herpes simplex virus strain lacking functional ICP27 and ICP34.5 genes and their use as vectors for the expression of heterologous therapeutic genes in nervous system disorders

INVENTOR(S): Coffin, Robert Stuart; Latchman, Seymour David; MacLean, Alasdair Roderick; Brown, Suzanne Moira

PATENT ASSIGNEE(S): Medical Research Council, UK; Coffin, Robert Stuart; Latchman, Seymour David; MacLean, Alasdair Roderick; Brown, Suzanne Moira

SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804726	A1	19980205	WO 1997-GB2017	19970725

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2262010	A1	19980205	CA 1997-2262010	19970725
AU 9737007	A	19980220	AU 1997-37007	19970725
AU 726645	B2	20001116		
EP 920523	A1	19990609	EP 1997-933762	19970725
EP 920523	B1	20031008		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000516809	T	20001219	JP 1998-508602	19970725
NZ 333901	A	20010525	NZ 1997-333901	19970725
AT 251672	T	20031015	AT 1997-933762	19970725
US 6248320	B1	20010619	US 1999-230479	19990610
PRIORITY APPLN. INFO.:			GB 1996-15794 A	19960726
			WO 1997-GB2017 W	19970725

AB The present invention provides a herpes simplex virus (HSV) strain which lacks a functional ICP34.5 gene and a functional ICP27 gene. HSV strains carrying inactivating mutations in both ICP34.5 and ICP27 genes exhibit greatly improved levels of expression of heterologous genes compared to virus strains carrying mutations in ICP34.5 alone. These doubly-mutated strains are also safer than strains carrying mutations in ICP27 alone. Also, an addnl. inactivating mutation in ICP4 and an inactivating mutation in VMW65, which abolishes its transcriptional activation activity, reduces further the toxicity of the viral strains. Thus, HSP strains which lack these genes are useful as vectors in the treatment of disorders of, or injuries to, the nervous system of a mammal.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:552065 CAPLUS
DOCUMENT NUMBER: 119:152065
TITLE: Mutant antiviral regulatory proteins
INVENTOR(S): Weber, Peter C.
PATENT ASSIGNEE(S): Penn State Research Foundation, USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9301301	A1	19930121	WO 1992-US5802	19920702
W: JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
PRIORITY APPLN. INFO.:			US 1991-726071 A	19910705

AB A dominant neg. mutant of a promiscuous viral transactivator protein was isolated in an attempt to generate a polypeptide which could inhibit gene expression and virus replication nonspecifically. This mutant, a truncated derivative of the herpes simplex 1 (HSV-1) regulatory protein ICP0 (infected cell polypeptide 0) comprising at least amino acids 1-245, behaved as a powerful repressor of gene expression from an assortment of HSV-1 and non-HSV-1 promoters in transient expression assays. It was also capable of inhibiting the replication of both HSV-1 and a completely unrelated virus, HIV, in cell culture. A dominant neg. mutant of VP16, another transactivator protein of HSV-1, also inhibited HSV-1 replication in Vero cells. This mutant may be useful in treating a wide variety of different viral infections in vivo.

L14 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:622497 CAPLUS
DOCUMENT NUMBER: 105:222497

TITLE: Co-ordinate regulation of herpes simplex virus gene expression is mediated by the functional interaction of two immediate early gene products
AUTHOR(S): Gelman, Irwin H.; Silverstein, Saul
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA
SOURCE: Journal of Molecular Biology (1986), 191(3), 395-409
CODEN: JMOBAK; ISSN: 0022-2836
DOCUMENT TYPE: Journal
LANGUAGE: English

AB At early times after infection with herpes simplex virus, transcription from β-promoters is initiated only in the presence of a functional 174,000 Mr phosphoprotein (ICP4), encoded by an immediate early (α) gene (IE4). A transient expression assay was used to analyze the requirement for 2 (ICP4 and ICP0) of the 5 α-gene products in the transcriptional regulation of model α and β-gene promoters. These studies reveal that cells cotransfected with plasmids containing the α-gene sequences for infected cell proteins (ICPs) 4 and 0 and a thymidine kinase (TK, a β-gene) gene or the thymidine kinase promoter fused to a chloramphenicol acetyltransferase (CAT) cassette accumulate 10-20-fold more RNA or exhibit 10-20-fold more CAT activity than cells cotransfected with a plasmid encoding either A-gene protein and a thymidine kinase indicator gene. Functional ICP4 is required for enhanced transcriptional activation in the transient expression assay system. It is also required for the uniform dispersal of ICP0 throughout the nucleus as shown by immunofluorescence staining anal. of transfected cells. Two α-promoter-CAT fusions were used as targets to study what effects ICP4, ICP0, and Vmw65 (the virion-associated α-gene transactivator) have on expression from α-promoters that contain all of the sequences that confer α-gene regulation, or only the core sequence governing basal level expression. It was concluded that ICP4 can activate α-gene expression from the core sequence and, depending on its abundance, activate or repress expression from a promoter containing the sequences required for α-gene regulation. Independent of these α-regulatory sequences, cotransfection with low levels of sequences encoding both ICP0 and ICP4 activate expression. At higher ratios of effector (both ICP4 and ICP0), the target accumulation of CAT activity decreases. Although a ts allele of IE4 (cloned from the mutant virus tsK) does not activate α-gene expression, it can enhance the ability of ICP0 to activate a target containing α-regulatory sequences. Virus studies involving tsK support the conclusion that functional ICP4 is required to activate β-promoters and to repress expression from α-promoters, and help to explain the pleiotropic effects of the tsK mutation. These analyses have also revealed the presence of a novel RNA species that overlaps the sequences encoding ICP0. Thus, co-ordinate regulation of HSV gene expression may be mediated by the functional interaction of at least 2 α-gene products, ICP0 and ICP4.

L14 ANSWER 5 OF 5 CAPLUS
ACCESSION NUMBER: 1986:124043 CAPLUS
DOCUMENT NUMBER: 104:124043
TITLE: Analysis of DNA sequences which regulate the transcription of herpes simplex virus immediate early gene 3: DNA sequences required for enhancer-like activity and response to trans-activation by a virion polypeptide
AUTHOR(S): Bzik, David J.; Preston, Chris M.
CORPORATE SOURCE: Virol. Unit, Med. Res. Counc., Glasgow, G11 5JR, UK
SOURCE: Nucleic Acids Research (1986), 14(2), 929-43
CODEN: NARHAD; ISSN: 0305-1048
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The far upstream region of herpes simplex virus (HSV) immediate

early (IE) gene 3 has previously been shown to increase gene expression in an enhancer-like manner, and to contain sequences which respond to stimulation of transcription by a virion polypeptide, Vmw65. To analyze the specific DNA sequences which mediate these functions, sequential deletions from each end of the far upstream region were made. The effects of the deletions on transcription in the absence or presence of the Vmw65 were measured by use of a transient expression assay. The enhancer-like activity was due to 3 separable elements, whereas 2 addnl. DNA regions were involved in the response to Vmw65. One of the responding elements corresponded to an AT-rich consensus (TAATGARATTC, where R=purine) present in all IE gene far upstream regions, and the other was a GA-rich sequence also present in IE genes 2 and 4/5. The TAATGARATTC element could mediate responsiveness to Vmw65 but it was fully active only in the presence of the GA-rich element. The GA-rich element was unable to confer a strong response alone but could activate an otherwise nonfunctional homolog of TAATGARATTC.

=> D L15 IBIB ABS 1-9

L15 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:464735 CAPLUS
DOCUMENT NUMBER: 144:64873
TITLE: Enhanced long-term expression from helper virus-free HSV-1 vectors packaged in the presence of deletions in genes that modulate the function of VP16, UL46 and UL47
AUTHOR(S): Liu, Meng; Tang, Ju; Wang, Xiaodan; Yang, Tianzhong; Geller, Alfred I.
CORPORATE SOURCE: Department of Neurology, VA Hospital/Harvard Medical School, W. Roxbury, MA, 02132, USA
SOURCE: Journal of Neuroscience Methods (2005), 145(1-2), 1-9
CODEN: JNMEDT; ISSN: 0165-0270
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Herpes simplex virus (HSV-1) gene expression is hypothesized to shut off recombinant gene expression from HSV-1 vectors, but in a helper virus-free HSV-1 vector system, a number of promoters support only short-term expression. Thus paradoxically, recombinant gene expression remains short-term in the absence of almost all (.apprx.99%) of the HSV-1 genome. To resolve this paradox, we hypothesize that specific HSV-1 proteins that affect the virion can shut off recombinant gene expression. In an earlier study, we examined the effects on recombinant gene expression of five different proteins that affect the HSV-1 virion. We found that vectors packaged in the presence of mutated vhs or US11 exhibited minimal changes in gene expression, vectors packaged in the presence of a mutated US3 supported improved gene transfer (nos. of cells at 4 days), and vectors packaged in the presence of mutated UL13 or VP16 supported improved long-term expression. The capability of the VP16 transcriptional complex to reduce gene expression deserves addnl. study because VP16 is a powerful enhancer that interacts with a number of cellular and viral proteins. In particular, UL46 and UL47 are known to modulate the effects of VP16 on immediate early promoters. In this study, we examined expression from a HSV-1 vector that contains a neuronal-specific promoter and was packaged in the presence of deletions in UL46, or UL47, or both UL46 and UL47. In the rat striatum, each of these vector stocks supported both improved gene transfer (nos. of cells at 4 days) and improved long-term expression (2 mo). Vectors packaged in the presence of a deletion in both UL46 and UL47 supported larger improvements in gene expression compared to vectors packaged in the presence of deletions in either gene alone. The implications of these results for strategies to improve long-term expression are

discussed.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1029788 CAPLUS
DOCUMENT NUMBER: 142:54603
TITLE: Spread and replication of and immune response to γ134.5-negative herpes simplex virus type 1 vectors in BALB/c mice
AUTHOR(S): Broberg, Eeva K.; Peltoniemi, Jutta; Nygardas, Michaela; Vahlberg, Tero; Roeyttae, Matias; Hukkanen, Veijo
CORPORATE SOURCE: Department of Virology, University of Turku, Turku, Finland
SOURCE: Journal of Virology (2004), 78(23), 13139-13152
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have previously shown that intracranial infection of herpes simplex virus type 1 (HSV-1) vector R8306 expressing interleukin-4 (IL-4) can abolish symptoms of exptl. autoimmune encephalomyelitis, which is used as a model for human multiple sclerosis (Broberg et al., 2001). The aim of the current study was to search for means other than intracranial injection to deliver HSV-derived vectors to the central nervous system of mice. We also aimed to study the replication efficiency of these vectors in nervous system tissues and to elucidate the effects of the viruses on the immune response. We studied the spread and replication of the following viruses with deletions in neurovirulence gene γ134.5: R3616, R849 (lacZ transgene), R3659 (alpha-tk), R8306 (murine IL-4 transgene), and R8308 (murine IL-10 transgene). The samples were taken from trigeminal ganglia and brains of BALB/c mice after corneal, intralabial, and intranasal infection, and the viral load was examined by viral culture, HSV DNA PCR, and VP16 reverse transcription (RT)-PCR. The results show that (i) intranasal infection was the most efficient means of spread to the central nervous system (CNS) besides intracranial injection; (ii) the viruses did not grow in the culture from the brain samples, but the viral DNA persisted even until day 21 postinfection; (iii) viral replication, as observed by VP16 mRNA RT-PCR, occurred mainly on days 4 and 7 postinfection in trigeminal ganglia and to a low extent in brain; (iv) R3659, R8306, and R8308 showed reactivation from the trigeminal ganglia in explant cultures; (v) in the brain, the vectors spread to the midbrain more efficiently than to other brain areas; and (vi) the deletions in the R3659 genome significantly limited the ability of this virus to replicate in the nervous system. The immunol. studies show that (i) the only recombinant to induce IL-4 mRNA expression in the brain was R8306, the gamma interferon response was very low in the brain for R3659 and R8306, and the IL-23p19 response to R8306 decreased by day 21 postinfection, unlike for the other viruses; (ii) Δγ134.5 HSV vectors modulated the subsets of the splenocytes differently depending on the transgene; (iii) R3659 infection of the nervous system induces expression and production of cytokines from the stimulated splenocytes; and (iv) HSV vectors expressing IL-4 or IL-10 induce expression and production of both of the Th2-type cytokines from splenocytes. We conclude that the intranasal route of infection is a possible means of delivery of Δγ134.5 HSV vectors to the CNS in addition to intracranial infection, although replication in the CNS remains minimal. The DNA of the HSV vectors is able to reside in the brain for at least 3 wk. The features of the immune response to the vectors must be considered and may be exploited in gene therapy expts. with these vectors.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:648545 CAPLUS
DOCUMENT NUMBER: 141:189640
TITLE: Novel Herpes simplex VP16 protein binding polypeptides, polynucleotides, antibodies and inhibitors/antagonists for diagnosis and treatment of infection by HSV, EBV or Kaposi sarcoma herpes virus
INVENTOR(S): Meisterernst, Michael; Mittler, Gerhard; Schaberg, Ulf; Stuehler, Thomas
PATENT ASSIGNEE(S): GSF- Forschungszentrum Fuer Umwelt Und Gesundheit, GmbH, Germany
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004067560	A2	20040812	WO 2004-EP681	20040127
WO 2004067560	A3	20050512		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI

PRIORITY APPLN. INFO.: US 2003-442517P P 20030127

AB The present invention relates to novel polypeptides capable of binding to Herpes simplex protein VP16 domain H1, and isolated polynucleotides encoding these polypeptides. The novel HSV VP16 H1 domain-binding polypeptides are hVaCID, mVaCID, DoCID and ACID. The invention also provide vectors, host cells, antibodies, and recombinant methods for producing these polypeptides. The invention further relates to methods for screening inhibitors/antagonists, activators/agonists and binding partners; and methods useful for diagnosing and treating Herpes simplex, EBV or Karposi Sarcoma Herpes Virus infections and disorders related to such infections.

L15 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:772779 CAPLUS
DOCUMENT NUMBER: 133:330523
TITLE: A herpes simplex virus type 1 (HSV -1)-derived vector with deletions in both LAT and ICP34.5 genes and its use in tumor therapy
INVENTOR(S): Weschler, Steven L.; Nesburn, Anthony B.; Perng, Guey-Chuen; Yu, John S.; Black, Keith L.
PATENT ASSIGNEE(S): Cedars-Sinai Medical Center, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000065078	A1	20001102	WO 2000-US11031	20000424

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,

SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6774119	B1	20040810	US 1999-299817	19990426
EP 1173598	A1	20020123	EP 2000-926327	20000424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002098170	A1	20020725	US 2001-46491	20011129
PRIORITY APPLN. INFO.:			US 1999-299817 A	19990426
			WO 2000-US11031 W	20000424

AB Disclosed is a method of selectively inhibiting the growth of malignant cells in mammals, including humans. The method selectively inhibits the growth of malignant cells of all varieties, and is particularly useful in treating brain tumors and other malignancies of the central nervous system. The method employs HSV-1-derived vectors containing a DNA having a deletion in both copies of the LAT gene and both copies of the ICP34.5 gene of HSV-1. The vectors are delivered to malignant cells either in vivo or in vitro, in accordance with the method. The HSV-1-derived expression vectors are non-neurovirulent and do not spontaneously reactivate from latency, and they optionally contain a functional HSV thymidine kinase gene, which can enhance the effectiveness against cancer of drug treatment with gancyclovir or acyclovir. Alternatively, the HSV-1-derived vectors contain at least one transcriptional unit of a LAT promoter sequence operatively linked to a nucleic acid having a nucleotide sequence encoding a polypeptide toxic for cells expressing the vector, for example, human interferon-γ. A method of expressing in a mammalian cell a gene encoding a preselected protein, a method of treating a genetic defect, and a method of detecting an HSV-1 expressing cell also employ vectors of the present invention that contain at least one transcriptional unit of a constitutive LAT promoter operatively linked to and controlling the transcription of a gene encoding a preselected protein. Also, disclosed are kits for expressing in a mammalian cell a gene encoding a preselected protein, useful for practicing the methods, and mammalian cells containing the HSV-derived vectors.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 9 CAPLUS

ACCESSION NUMBER: 1999:673791 CAPLUS
DOCUMENT NUMBER: 132:9567
TITLE: Transcriptional regulation of the VP16 gene of herpes simplex virus type 1
AUTHOR(S): Kwun, Hyun Jin; Jun, Hong Ki; Lee, Tae Ho; Jang, Kyung Lib
CORPORATE SOURCE: Department of Microbiology, College of Natural Sciences, Pusan National University, Pusan, 609-735, S. Korea
SOURCE: Journal of Biochemistry and Molecular Biology (1999), 32(5), 456-460
CODEN: JBMBE5; ISSN: 1225-8687
PUBLISHER: Springer-Verlag Singapore Pte. Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The promoter of the HSV-1 VP16 gene contains binding sites for the cellular transcription factors such as USF, CTF, and Sp1, each of which affects basal level expression of the VP16 gene. Transcription of the VP16 gene was induced by viral immediate-early proteins, ICP0 and ICP4, in a synergistic manner but repressed by ICP22. To gain further insight into the role of ICP0 in the expression of the VP16 gene during virus infection, several mutants with deletions in each of their transcriptional

regulatory elements were generated. According to transient gene expression assays of these mutants using the CAT gene as a reporter, the USF and CTF binding sites were necessary for efficient induction of the promoter in the presence of transfected ICP0 or during virus infection, whereas the Sp1 binding site had little effect on ICP0-mediated VP16 expression. These results indicate that the immediate early proteins of HSV-1 regulate expression of the VP16 gene during virus infection by modulating the activities of cellular transcription factors such as USF and CTF.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:465467 CAPLUS
DOCUMENT NUMBER: 127:172797
TITLE: Truncation of the C-terminal acidic transcriptional activation domain of herpes simplex virus VP16 produces a phenotype similar to that of the in1814 linker insertion mutation
AUTHOR(S): Smiley, James R.; Duncan, Joanne
CORPORATE SOURCE: Cancer Research Group, Institute for Molecular Biology and Biotechnology, Pathology Dep., McMaster University, Hamilton, ON, L8N 3Z5, Can.
SOURCE: Journal of Virology (1997), 71(8), 6191-6193
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We examined the phenotype of a herpes simplex virus (HSV) type 1 mutant (V422) in which the C-terminal acidic activation domain of the virion transactivator VP16 is truncated at residue 422. The efficacy of plaque formation by V422 on Vero cells was boosted by approx. 100-fold by including hexamethylene bisacetamide (HMBA) in the growth medium, as previously observed with the in1814 VP16 linker insertion mutant isolated by Preston and colleagues. V422 displayed severely reduced levels of the immediate-early transcripts encoding ICP0 and ICP4 during infection in the presence of cycloheximide, and this defect was partially overcome by the addition of HMBA. The defect in plaque formation exhibited by V422 and in1814 was efficiently complemented in U2OS osteosarcoma cells, which had previously been shown to complement ICP0 null mutations. Taken in combination, these data confirm the key role of VP16 in triggering the onset of the HSV lytic cycle.

L15 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:568171 CAPLUS
DOCUMENT NUMBER: 123:163668
TITLE: The regulation of synthesis and properties of the protein product of open reading frame P of the herpes simplex virus 1 genome
AUTHOR(S): Lagunoff, Michael; Roizman, Bernard
CORPORATE SOURCE: Marjorie B. Kovler Viral Oncology Lab., Univ. Chicago, Chicago, IL, 60637, USA
SOURCE: Journal of Virology (1995), 69(6), 3615-23
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Open reading frame P (ORF P) maps in the inverted repeat sequence ab and b'a' flanking the long unique (UL) sequence of the herpes simplex virus 1 genome, within the sequence reported to be transcribed during latent infection of sensory neurons. Both the protein and the RNA were previously reported to be expressed only in cells infected with a deletion mutant or with a mutant carrying a ts lesion in the α 4 gene encoding the infected cell protein number 4

(ICP4), a major regulatory protein of the virus. In this report we show that (1) disruption of the ICP4 DNA binding site by replacement mutagenesis resulted in the overexpression of ORF P protein even at permissive temps., leading to productive infection; (2) the expression of ORF P does not require prior viral protein synthesis; (3) late in infection the ORF protein P is processed into multiple forms characterized by a slower electrophoretic mobility in denaturing gels; (4) ORF P protein accumulates in nuclei of infected cells; and (5) in some nuclei of infected cells, ORF P protein is organized in the form of rods traversing the nucleus from the basolateral to the apical side. We conclude that ORF P has many of the properties predictive of a viral gene group, which we designate pre-α. Specifically, these could be induced by the α transinducing factor (also known as VP16) carried in the virion; they would be firmly shut off by the onset of expression of α genes required for productive infection; and in the absence of repressive effects of ICP4, their expression could be dependent on the number of viral DNA copies available for transcription. Finally, the productively induced cell would evolve a way of disposing excess pre-α proteins by posttranslational processing.

L15 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:595885 CAPLUS
DOCUMENT NUMBER: 121:195885
TITLE: Improved cell survival by the reduction of immediate-early gene expression in replication-defective mutants of herpes simplex virus type 1 but not by mutation of the virion host shutoff function
AUTHOR(S): Johnson, Paul A.; Wang, Ming Jing; Friedmann, Theodore
CORPORATE SOURCE: Cent. for Mol. Genetics, Univ. California, La Jolla, CA, 92093-0634, USA
SOURCE: Journal of Virology (1994), 68(10), 6347-62
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Derivs. of herpes simplex virus type 1 (HSV-1) have elicited considerable interest as gene transfer vectors because of their ability to infect a wide range of cell types efficiently, including fully differentiated neurons. However, it has been found that infection of many types of cell with vectors derived from replication-defective mutants of HSV-1 is associated with cytopathic effects (CPE). The authors have previously shown that viral gene expression played an important role in the induction of CPE caused by an HSV-1 mutant deleted for the essential immediate-early gene 3 (IE 3) (P. A. Johnson, A. Miyanohara, F. Levin, T. Cahill, and T. Friedmann, J. Virol. 66:2952-2965, 1992). The authors have investigated which viral genes might be responsible for CPE by comparing the ability of each of the individual genes expressed by an IE 3 deletion mutant during a nonproductive infection to inhibit biochem. transformation after cotransfection of BHK or CV-1 cells with a selectable marker gene. Transfection of IE genes 1, 2, and 4 individually all caused a marked inhibition of colony formation, while transfection of IE 5 and the large subunit of ribonucleotide reductase had little effect. These results suggested that it would be necessary to mutate or reduce the expression of nearly all HSV-1 IE genes to reduce virus-induced CPE. Therefore, the authors have used VP16 mutants, which are unable to transinduce IE gene expression (C. I. Ace, T. A. McKee, J. M. Ryan, J. M. Cameron, and C. M. Preston, J. Virol. 63:2260-2269, 1989), to derive two replication-defective strains: 14HΔ3, which is deleted for both copies of IE 3, and in 1850Δ42, which has a deletion in the essential early gene UL42. The IE 3-VP16 double mutant, 14HΔ3, is significantly less toxic than a single IE 3 deletion mutant over a range of multiplicities of infection, as measured in a cell-killing assay, and has an enhanced ability to persist in infected cells in a biol.

retrievable form. In contrast, the UL42-VP16 double mutant, in 1850Δ42, showed reduced toxicity only at low multiplicities of infection. To test the role of the virion host shutoff function as an addnl. candidate to influence virus-induced CPE, the authors have introduced a large insertion mutation into the virion host shutoff gene of an IE 3 deletion mutant and the double mutant 14HΔ3. Mutation of this gene did not reduce the cytotoxicity of either strain. These results demonstrate that long-term survival of cells infected with replication-defective HSV-1 mutants can be enhanced through genetic manipulations that reduce viral gene expression.

L15 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:532855 CAPLUS
DOCUMENT NUMBER: 119:132855
TITLE: The transcriptional activation domain of varicella-zoster virus open reading frame 62 protein is not conserved with its herpes simplex virus homolog
AUTHOR(S): Cohen, Jeffrey I.; Heffel, Dominic; Seidel, Karen
CORPORATE SOURCE: Lab. Clin. Invest., Natl. Inst. Allergy Infect. Dis., Bethesda, MD, 20892, USA
SOURCE: Journal of Virology (1993), 67(7), 4246-51
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Varicella-zoster virus (VZV) open reading frame 62 (ORF62) encodes an immediate-early protein that transactivates expression of VZV, herpes simplex virus (HSV), and cellular genes in transient expression assays. VZV ORF62 is homologous to HSV ICP4 and pseudorabies virus immediate-early (IE180) proteins. All three viral proteins have conserved DNA binding domains that recognize similar sites in their corresponding promoters. Here, the authors show that the transcriptional activation domain of ORF62 is located near the amino terminus of the protein and is not conserved with the activation domain of ICP4. A 161-amino-acid activation domain of ORF62 activates transcription to a level comparable to that of the potent HSV VP16 activation domain; much of the activity is contained in the first 90 amino acids of ORF62. Deletion of the activation domain from full-length ORF62 markedly reduced transactivating activity. These expts. indicate that while VZV ORF62 and HSV ICP4 have conserved amino acid sequences, including their DNA binding domains, the transcriptional activation domains are poorly conserved.

=> D L13 IBIB ABS 1-11

L13 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:803532 CAPLUS
DOCUMENT NUMBER: 142:1579
TITLE: Immediate-early expression of the herpes simplex virus type 1 ICP27 transcript is not critical for efficient replication in vitro or in vivo
AUTHOR(S): Sun, Aixu; Devi-Rao, G. V.; Rice, M. K.; Gary, L. W.; Bloom, D. C.; Sandri-Goldin, R. M.; Ghazal, P.; Wagner, E. K.
CORPORATE SOURCE: Department of Molecular Biology and Biochemistry, University of California, Irvine, CA, USA
SOURCE: Journal of Virology (2004), 78(19), 10470-10478
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We constructed a promoter mutation altering the immediate-early expression of the herpes simplex virus type 1 (HSV-1) ICP27 transcript and its cognate wild-type rescue viruses in order to assess the

role of the ICP27 protein in the earliest stages of viral infection by global transcriptional anal. with a DNA microarray. This mutant, ICP27/VP16, replaces the whole ICP27 promoter/enhancer with the VP16 promoter. It demonstrates loss of immediate-early expression of ICP27 according to the criteria expression in the absence of de novo protein synthesis and earliest expression in the kinetic cascade. Significant differences in relative transcript abundances between the mutant and wild-type rescue viruses were limited at the earliest times measured and not evident at all by 4 h after infection. Consistent with this observation, levels of some critical proteins were reduced in the mutant as compared to rescue virus infections at the earliest times tested, but were equivalent by 8 h postinfection. Further, both single and multistep levels of virus replication were equivalent with both mutant and rescue viruses. Thus, altering the immediate-early kinetics of ICP27 leads to a suboptimal quant. lag phase in gene expression but without consequence for replication fitness in vitro. Infections in vivo also revealed equivalent ability of mutant and rescue viruses to invade the central nervous system of mice following footpad injections. Limitations to an immediate-early role of ICP27 in the biol. of HSV are discussed in light of these observations.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:648545 CAPLUS
DOCUMENT NUMBER: 141:189640
TITLE: Novel Herpes simplex VP16 protein binding polypeptides, polynucleotides, antibodies and inhibitors/antagonists for diagnosis and treatment of infection by HSV, EBV or Kaposi sarcoma herpes virus
INVENTOR(S): Meisterernst, Michael; Mittler, Gerhard; Schaberg, Ulf; Stuehler, Thomas
PATENT ASSIGNEE(S): GSF- Forschungszentrum Fuer Umwelt Und Gesundheit, GmbH, Germany
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004067560	A2	20040812	WO 2004-EP681	20040127
WO 2004067560	A3	20050512		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI

PRIORITY APPLN. INFO.: US 2003-442517P P 20030127

AB The present invention relates to novel polypeptides capable of binding to Herpes simplex protein VP16 domain H1, and isolated polynucleotides encoding these polypeptides. The novel HSV VP16 H1 domain-binding polypeptides are hVaCID, mVaCID, DoCID and ACID. The invention also provide vectors, host cells, antibodies, and recombinant methods for producing these polypeptides. The invention further relates to methods for screening inhibitors/antagonists, activators/agonists and binding partners; and methods useful for diagnosing and treating Herpes simplex, EBV or Karposi Sarcoma Herpes Virus infections and disorders related to such infections.

L13 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:633469 CAPLUS

DOCUMENT NUMBER: 141:168975
TITLE: Herpesvirus amplicon particles capable of integrating into chromosomes of dividing and non-dividing cell types and their therapeutic uses
INVENTOR(S): Federoff, Howard J.; Halterman, Marc W.; Bowers, William J.
PATENT ASSIGNEE(S): University of Rochester, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004064765	A2	20040805	WO 2004-US1821	20040123
WO 2004064765	A3	20050428		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
AU 2004206967	A1	20040805	AU 2004-206967	20040123
CA 2513559	A1	20040805	CA 2004-2513559	20040123
EP 1592455	A2	20051109	EP 2004-704851	20040123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006239970	A1	20061026	US 2006-543216	20060607
PRIORITY APPLN. INFO.:			US 2003-442030P P	20030123
			WO 2004-US1821 W	20040123

AB The invention includes methods for delivering therapeutic agents to a patient through administration of herpesvirus amplicon particles generated by a cell that stably expresses herpes simplex virus (HSV) immediate early 3 (IE3) gene. The cell is also infected with a helper virus containing mutations in VP16 or VHS protein genes, plasmids expressing VP16 or VHS proteins in trans, a plasmid expressing a therapeutic transgene, and a plasmid expressing Sleeping Beauty transposase. In addition, the invention claims therapeutic use of the herpesvirus amplicons against cancer, particularly leukemia, and therapeutic use against Creutzfeldt-Jacob disease. The invention further claims use of herpesvirus amplicon particles for expression of antigens and for expression of proteins that protect spiral ganglion neurons, the latter for prevention of hearing loss. Examples of the invention show addition of VP16 in trans improves amplicon titers independently of canonical cis elements and the mutant HSV-1 amplicon showed reduced toxicity towards neuronal cell cultures. The integrating HSV-1 amplicon vectors were produced using the synthetic, Tc1-like Sleeping Beauty transposition system. Newborn mice were injected in the central nervous system with the HSV amplicon vectors and 90 days later, striata from the mice were shown to express a lacZ transgene.

L13 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:472957 CAPLUS
DOCUMENT NUMBER: 135:56907
TITLE: Replication incompetent herpes viruses for use in gene therapy of peripheral nervous system disorders
INVENTOR(S): Coffin, Robert Stuart
PATENT ASSIGNEE(S): Biovex Ltd., UK
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046450	A1	20010628	WO 2000-GB4983	20001222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2395578	A1	20010628	CA 2000-2395578	20001222
EP 1246930	A1	20021009	EP 2000-985689	20001222
EP 1246930	B1	20051109		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518081	T	20030603	JP 2001-546946	20001222
AT 309384	T	20051115	AT 2000-985689	20001222
AU 783691	B2	20051124	AU 2001-22088	20001222
US 2003040500	A1	20030227	US 2002-168801	20020911
PRIORITY APPLN. INFO.:			GB 1999-30419 A	19991222
			WO 2000-GB4983 W	20001222

AB The invention relates to replication incompetent herpes simplex viruses (HSV) capable of efficiently transferring genes to multiple sites within the nervous system for use in gene therapy. Highly disabled HSV vectors which cannot replicate in any cell other then those used to prepare vector stocks (i.e. essential genes have been inactivated in the vector which are complemented in the producer cell line) can give highly efficient gene delivery to the peripheral nervous system following direct injection into peripheral nerve. A replication incompetent HSV comprises: (a) a mutation which prevents or reduces the expression of at least two immediate early genes; and (b) a heterologous gene, which encodes a therapeutic protein, operably linked to a promoter active during herpes virus latency. The invention provides use of a replication incompetent HSV in the manufacture of a medicament for use in treating or preventing a peripheral nervous system disorder by administering said medicament to a peripheral nerve, in a method of determining whether a transgene has an effect on a phenotype associated with a peripheral nervous system disorder and in a method of treatment of a disorder of the peripheral nervous system.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:455574 CAPLUS

DOCUMENT NUMBER: 135:192780

TITLE: ICP0, ICP4, or VP16 expressed from adenovirus vectors induces reactivation of latent Herpes simplex virus type 1 in primary cultures of latently infected trigeminal ganglion cells

AUTHOR(S): Halford, William P.; Kemp, Clinton D.; Isler, Jennifer A.; Davido, David J.; Schaffer, Priscilla A.

CORPORATE SOURCE: Department of Microbiology, University of Pennsylvania School of Medicine, Philadelphia, PA, 19104, USA

SOURCE: Journal of Virology (2001), 75(13), 6143-6153
CODEN: JOVIAM; ISSN: 0022-538X

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In a previous study, we demonstrated that infected-cell polypeptide 0 (ICP0) is necessary for the efficient reactivation of herpes simplex virus type 1 (HSV-1) in primary cultures of latently infected

trigeminal ganglion (TG) cells. The present study was undertaken to determine whether ICP0 is sufficient to trigger HSV-1 reactivation in latently infected TG cells. To test this hypothesis, replication-defective adenovirus vectors that express wild-type and mutant forms of ICP0 under the control of a tetracycline response element (TRE) promoter were constructed. Similar adenovirus vectors encoding wild-type ICP4, wild-type and mutant forms of the HSV-1 origin-binding protein (OBP), and wild-type and mutant forms of VP16 were also constructed. The TRE promoter was induced by coinfection of Vero cells with the test vector and an adenovirus vector that expresses the reverse tetracycline-regulated transactivator in the presence of doxycycline. Northern blot anal. demonstrated that transcription of the OBP gene in the adenovirus expression vector increased as a function of doxycycline concentration over a range of 0.1 to 10 μM. Likewise, Western blot anal. demonstrated that addition of 3 μM doxycycline to adenovirus vector-infected Vero cells resulted in a 100-fold increase in OBP expression. Wild-type forms of ICP0, ICP4, OBP, and VP16 expressed from adenovirus vectors were functional based on their ability to complement plaque formation in Vero cells by replication-defective HSV-1 strains with mutations in these genes. Adenovirus vectors that express wild-type forms of ICP0, ICP4, or VP16 induced reactivation of HSV-1 in 86% ± 5%, 86% ± 5%, and 97% ± 5% of TG cell cultures, resp. (means ± standard deviations). In contrast, vectors that express wild-type OBP or mutant forms of ICP0, OBP, or VP16 induced reactivation in 5% ± 5%, 8% ± 0%, 0% ± 0%, and 13% ± 6% of TG cell cultures, resp. In control infections, an adenovirus vector expressed green fluorescent protein efficiently in TG neurons but did not induce HSV-1 reactivation. Therefore, expression of ICP0, ICP4, or VP16 is sufficient to induce HSV-1 reactivation in latently infected TG cell cultures. We conclude that this system provides a powerful tool for determining which cellular and viral proteins are sufficient to induce HSV-1 reactivation from neuronal latency.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:90458 CAPLUS
DOCUMENT NUMBER: 130:149531
TITLE: Culture and genetic transformation of endothelial cells for use in gene therapy and prophylaxis of disease
INVENTOR(S): Havemann, Klaus; Muller, Rolf; Sedlacek, Hans-Harald
PATENT ASSIGNEE(S): Hoechst Marion Roussel Deutschland GmbH, Germany
SOURCE: Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 893493	A2	19990127	EP 1998-113137	19980715
EP 893493	A3	20021204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19731154	A1	19990128	DE 1997-19731154	19970721
DE 19731154	C2	20000210		
IN 1998MA01607	A	20050304	IN 1998-MA1607	19980717
CA 2237698	A1	19990121	CA 1998-2237698	19980720
AU 9877466	A	19990204	AU 1998-77466	19980720
AU 757960	B2	20030313		

HU 9801634	A2	19990628	HU 1998-1634		19980720
RU 2205029	C2	20030527	RU 1998-113791		19980720
CN 1206044	A	19990127	CN 1998-116131		19980721
JP 11089587	A	19990406	JP 1998-205261		19980721
BR 9802542	A	20000111	BR 1998-2542		19980721
US 2002098166	A1	20020725	US 1998-119659		19980721
PRIORITY APPLN. INFO.:			DE 1997-19731154	A	19970721
			DE 1997-19752299	A	19971126

AB The invention concerns the preparation of transduced endothelial cells for gene therapy and prophylaxis. Cells are isolated from blood or other cell containing body fluids; they are cultured on media containing gangliosides, phospholipids, glycopeptides, and/or growth hormones, that influence the differentiation, survival, migration and/or the vascularization of the cells. Cells are immortalized by oncogene transformation, by activation of an oncogene or by the inactivation of a tumor suppressor gene. Cells are transfected with a plasmid responsible for the gene therapy containing an effector gene that is activated by promoters; activation of the promoters depends either on the target cell, the cell cycle, a virus and/or hypoxia. The cells can be applied for the production of pharmaceuticals for the therapy of various diseases. Oncogenes are mutations of cdk-4 , cdk-6 and cdk-2, e.g. a mutation of cdk-4 at codon 24 that results in the coding of Cys instead of Arg. For the inactivation of retinoblastoma protein suppressor gene, the gene is coding for the adenovirus E1A-protein, SV40 large T-antigen, papillomavirus E-7 protein and a 23 amino acid peptide sequence. Effector genes code for a biol. active substance, e. g. cytokines, chemokines, growth hormones, receptors, cytostatic agents, or for an enzyme that splits a pharmacon precursor into a pharmacon. Isolated endothelial cells were transformed with a plasmid that contained the promoter of the human endoglin gene, the cDNA of the cyclin dependent kinase-4 (cdk-4) with a mutation at codon 24, and the SV40 nuclear localization signal (NLS). Further transformation consisted of a plasmid with activator subunits, activator responsive promoter and effector gene. One of the activator subunits contained the promoter of cdc25C gene, the SV40 NLS, acidic transactivation domains (TAS) of HSV-1 VP16, and cDNA for the cytoplasmic fragment of the CD4 glycoprotein; the other activator subunit contains the promoter of the human endoglin gene, the SV40 NLS, the cDNA for the DNA binding domain of the GAl4 protein, and the cDNA for the CD4 binding sequence of the p56 Ick protein. The activator-responsive promoter includes 10x the binding sequence of the Gal4-binding protein consisting of 16 nucleotides and the SV40 basal promoter. This promoter was used to drive expression of a β-glucuronidase reporter gene. Expression of the gene was greater in cells that had undergone replication than in cells in G0/G1 cells.

L13 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:239298 CAPLUS
DOCUMENT NUMBER: 128:279564
TITLE: Herpes simplex virus attenuated strains with modified immediate early genes
INVENTOR(S): DeLuca, Neal A.
PATENT ASSIGNEE(S): University of Pittsburgh of the Commonwealth System of Higher Education, USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815637	A1	19980416	WO 1997-US8681	19970522
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				

DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB,
GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
ML, MR, NE, SN, TD, TG

US 5804413	A	19980908	US 1996-651419	19960522
CA 2255939	A1	19980416	CA 1997-2255939	19970522
AU 9731379	A	19980505	AU 1997-31379	19970522
EP 904395	A1	19990331	EP 1997-926668	19970522
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, IE, FI				
JP 2001503611	T	20010321	JP 1998-512036	19970522
US 6261552	B1	20010717	US 1998-194274	19981120
US 2001026799	A1	20011004	US 2001-829839	20010410
US 2003206888	A1	20031106	US 2003-427739	20030501
US 7078029	B2	20060718		

PRIORITY APPLN. INFO.:	US 1996-651419	A2 19960522
	US 1992-922839	B1 19920731
	US 1994-342795	A2 19941121
	US 1995-479024	A2 19950607
	WO 1997-US8681	W 19970522
	US 1998-194274	A1 19981120
	US 2001-829839	B1 20010410

AB The present invention provides an HSV having a genome from which, in the presence of the ICP4 gene product, a native immediate early gene is expressed with delayed kinetics, and an HSV having a genome with a mutation in each of the genes encoding ICP4, ICP27, and another HSV gene. Preferably, such HSV will also encode one or more exogenous genes. The present invention further provides a method of expressing a polynucleotide within a cell comprising infecting the cell with such an HSV. Furthermore, the present invention provides a cell line having DNA encoding the HSV proteins ICP4, ICP27, and ICP0, and a method of producing an HSV vector by employing such a cell line. The expression kinetics of any or all of the immediate early gene products can be delayed, such that the vector avoids the .apprx.5-10-fold decrease in viral titer associated with their expression in packaging cell lines. Attenuated immediate early gene expression can be achieved by mutation of viral sequences comprising the VP16-Oct1 consensus TAATGARAT sequence present within the inverted repeat regions of the HSV genome. These HSV mutant strains have characteristics amenable to use as gene transfer vehicles, including (1) the ability to obtain large quantities of recombinant virus, (2) a significant reduction in wild-type reversion, (3) an ability to accept larger foreign DNA fragments for gene transfer applications, (4) minimized interference with host cell protein synthesis, and (5) reduced or even minimal host cell cytotoxicity.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1997:465467 CAPLUS
DOCUMENT NUMBER:	127:172797
TITLE:	Truncation of the C-terminal acidic transcriptional activation domain of herpes simplex virus VP16 produces a phenotype similar to that of the in1814 linker insertion mutation
AUTHOR(S):	Smiley, James R.; Duncan, Joanne
CORPORATE SOURCE:	Cancer Research Group, Institute for Molecular Biology and Biotechnology, Pathology Dep., McMaster University, Hamilton, ON, L8N 3Z5, Can.
SOURCE:	Journal of Virology (1997), 71(8), 6191-6193 CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER:	American Society for Microbiology

DOCUMENT TYPE: Journal
LANGUAGE: English
AB We examined the phenotype of a herpes simplex virus (HSV) type 1 mutant (V422) in which the C-terminal acidic activation domain of the virion transactivator VP16 is truncated at residue 422. The efficacy of plaque formation by V422 on Vero cells was boosted by approx. 100-fold by including hexamethylene bisacetamide (HMBA) in the growth medium, as previously observed with the in1814 VP16 linker insertion mutant isolated by Preston and colleagues. V422 displayed severely reduced levels of the immediate-early transcripts encoding ICP0 and ICP4 during infection in the presence of cycloheximide, and this defect was partially overcome by the addition of HMBA. The defect in plaque formation exhibited by V422 and in1814 was efficiently complemented in U2OS osteosarcoma cells, which had previously been shown to complement ICP0 null mutations. Taken in combination, these data confirm the key role of VP16 in triggering the onset of the HSV lytic cycle.

L13 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:411026 CAPLUS
DOCUMENT NUMBER: 122:283736
TITLE: The Oct-1 POU domain stimulates adenovirus DNA replication by a direct interaction between the viral precursor terminal protein-DNA polymerase complex and the POU homeodomain
AUTHOR(S): Coenjaerts, Frank E. J.; van Oosterhout, Joost A. W. M.; van der Vliet, Peter C.
CORPORATE SOURCE: Lab. Physiological Chem., University Utrecht, Utrecht, 3508 TA, Neth.
SOURCE: EMBO Journal (1994), 13(22), 5401-9
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The bipartite POU domain of transcription factor Oct-1 stimulates adenovirus DNA replication through an interaction with the octamer sequence present in the auxiliary origin. An immobilized in vitro DNA replication system was employed to show that the POU domain enhances the formation of a pre-initiation complex composed of the viral precursor terminal protein-DNA polymerase (pTP-pol) complex and the origin. To investigate the mechanism of stimulation protein-protein interactions between the POU domain and the pTP-pol complex were explored. Such an interaction could be detected using a GST-POU fusion protein bound to glutathione-agarose beads. Binding was also observed with the POU homeodomain (POUHD), albeit weaker than with the intact POU domain, but not with the POU-specific subdomain. Four point mutations localized in the POUHD were analyzed for pTP-pol binding. Two of these, E22A and E30A, bound pTP-pol equally as well as the wild-type, whereas the other two, Q24A and E29A, were able to bind 2-4-fold better. These mutations are localized in the same region where the HSV transactivator VP16 binds, but did not coincide with the VP16 contacts. A direct correlation between pTP-pol binding and stimulation of DNA replication in vitro was observed for all mutants, suggesting that stimulation by the POU domain is caused by an interaction with the viral pTP-pol complex.

L13 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:595885 CAPLUS
DOCUMENT NUMBER: 121:195885
TITLE: Improved cell survival by the reduction of immediate-early gene expression in replication-defective mutants of herpes simplex virus type 1 but not by mutation of the virion host shutoff function

AUTHOR(S): Johnson, Paul A.; Wang, Ming Jing; Friedmann, Theodore
CORPORATE SOURCE: Cent. for Mol. Genetics, Univ. California, La Jolla, CA, 92093-0634, USA
SOURCE: Journal of Virology (1994), 68(10), 6347-62
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Derivs. of herpes simplex virus type 1 (HSV-1) have elicited considerable interest as gene transfer vectors because of their ability to infect a wide range of cell types efficiently, including fully differentiated neurons. However, it has been found that infection of many types of cell with vectors derived from replication-defective mutants of HSV-1 is associated with cytopathic effects (CPE). The authors have previously shown that viral gene expression played an important role in the induction of CPE caused by an HSV-1 mutant deleted for the essential immediate-early gene 3 (IE 3) (P. A. Johnson, A. Miyanohara, F. Levin, T. Cahill, and T. Friedmann, J. Virol. 66:2952-2965, 1992). The authors have investigated which viral genes might be responsible for CPE by comparing the ability of each of the individual genes expressed by an IE 3 deletion mutant during a nonproductive infection to inhibit biochem. transformation after cotransfection of BHK or CV-1 cells with a selectable marker gene. Transfection of IE genes 1, 2, and 4 individually all caused a marked inhibition of colony formation, while transfection of IE 5 and the large subunit of ribonucleotide reductase had little effect. These results suggested that it would be necessary to mutate or reduce the expression of nearly all HSV-1 IE genes to reduce virus-induced CPE. Therefore, the authors have used VP16 mutants, which are unable to transinduce IE gene expression (C. I. Ace, T. A. McKee, J. M. Ryan, J. M. Cameron, and C. M. Preston, J. Virol. 63:2260-2269, 1989), to derive two replication-defective strains: 14HΔ3, which is deleted for both copies of IE 3, and in 1850Δ42, which has a deletion in the essential early gene UL42. The IE 3-VP16 double mutant, 14HΔ3, is significantly less toxic than a single IE 3 deletion mutant over a range of multiplicities of infection, as measured in a cell-killing assay, and has an enhanced ability to persist in infected cells in a biol. retrievable form. In contrast, the UL42-VP16 double mutant, in 1850Δ42, showed reduced toxicity only at low multiplicities of infection. To test the role of the virion host shutoff function as an addnl. candidate to influence virus-induced CPE, the authors have introduced a large insertion mutation into the virion host shutoff gene of an IE 3 deletion mutant and the double mutant 14HΔ3. Mutation of this gene did not reduce the cytotoxicity of either strain. These results demonstrate that long-term survival of cells infected with replication-defective HSV-1 mutants can be enhanced through genetic manipulations that reduce viral gene expression.

L13 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:100543 CAPLUS
DOCUMENT NUMBER: 116:100543
TITLE: The herpes simplex virus trans-activator VP16 recognizes the Oct-1 homeo domain: evidence for a homeo domain recognition subdomain
AUTHOR(S): Stern, Seth; Herr, Winship
CORPORATE SOURCE: Cold Spring Harbor Lab., Cold Spring Harbor, NY, 11724, USA
SOURCE: Genes & Development (1991), 5(12B), 2555-66
CODEN: GEDEEP; ISSN: 0890-9369
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The homeo domain of the Oct-1 transcription factor directs formation of a multiprotein-DNA complex containing Oct-1, the herpes simplex virus (HSV) trans-activator VP16, and a 2nd host cell factor (HCF). This VP16-induced complex alters the regulatory activity of Oct-1, in part, by

associating it with the potent VP16 acidic transcriptional activation domain. Here, it is shown, that in the absence of HCF, VP16 can recognize specifically the Oct-1 homeo domain. A region of VP16 near the acidic activation domain appears to be involved exclusively in homeo domain recognition because a 4-amino-acid insertion within this region only affects the ability of VP16 to interact with Oct-1, leaving its DNA- and HCF-binding activities unchanged. A 33-amino-acid peptide containing this region complexes with the Oct-1 POU domain bound to DNA, suggesting that this VP16 region contains an autonomous homeo domain recognition subdomain. A.

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L12 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:464735 CAPLUS
DOCUMENT NUMBER: 144:64873
TITLE: Enhanced long-term expression from helper virus-free HSV-1 vectors packaged in the presence of deletions in genes that modulate the function of VP16, UL46 and UL47
AUTHOR(S): Liu, Meng; Tang, Ju; Wang, Xiaodan; Yang, Tianzhong; Geller, Alfred I.
CORPORATE SOURCE: Department of Neurology, VA Hospital/Harvard Medical School, W. Roxbury, MA, 02132, USA
SOURCE: Journal of Neuroscience Methods (2005), 145(1-2), 1-9
CODEN: JNMEDT; ISSN: 0165-0270
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Herpes simplex virus (HSV-1) gene expression is hypothesized to shut off recombinant gene expression from HSV-1 vectors, but in a helper virus-free HSV-1 vector system, a number of promoters support only short-term expression. Thus paradoxically, recombinant gene expression remains short-term in the absence of almost all (.apprx.99%) of the HSV-1 genome. To resolve this paradox, we hypothesize that specific HSV-1 proteins that affect the virion can shut off recombinant gene expression. In an earlier study, we examined the effects on recombinant gene expression of five different proteins that affect the HSV-1 virion. We found that vectors packaged in the presence of mutated vhs or US11 exhibited minimal changes in gene expression, vectors packaged in the presence of a mutated US3 supported improved gene transfer (nos. of cells at 4 days), and vectors packaged in the presence of mutated UL13 or VP16 supported improved long-term expression. The capability of the VP16 transcriptional complex to reduce gene expression deserves addnl. study because VP16 is a powerful enhancer that interacts with a number of cellular and viral proteins. In particular, UL46 and UL47 are known to modulate the effects of VP16 on immediate early promoters. In this study, we examined expression from a HSV-1 vector that contains a neuronal-specific promoter and was packaged in the presence of deletions in UL46, or UL47, or both UL46 and UL47. In the rat striatum, each of these vector stocks supported both improved gene transfer (nos. of cells at 4 days) and improved long-term expression (2 mo). Vectors packaged in the presence of a deletion in both UL46 and UL47 supported larger improvements in gene expression compared to vectors packaged in the presence of deletions in either gene alone. The implications of these results for strategies to improve long-term expression are discussed.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1029788 CAPLUS